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| 10/004,413 | 12/06/2001 | Neil W. Boaz | 039592-5113-01 | 8373 |

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| EXAMINER |
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OH, TAYLOR V

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| ART UNIT | PAPER NUMBER |
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1625

DATE MAILED: 04/18/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

| | | | |
|-----------------|------------------|--------------|-------------|
| Application No. | 10/004,413 | Applicant(s) | BOAZ ET AL. |
| Examiner | Taylor Victor Oh | Art Unit | 1625 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 06 December 2001.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 22-35 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 22-35 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3

4) Interview Summary (PTO-413) Paper No(s). _____

5) Notice of Informal Patent Application (PTO-152)

6) Other: _____

Specification

The disclosure is objected to because of the following informalities: a phrase " a C₄-C₁₀ aryl or heteroaryl group" line 8 on page 5, and line 3 on page 10 is written. However, this is vague and indefinite as to the range of the carbon atoms in the aryl group. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 22, 29, 31, 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nitro-aromatic carboxylic ester , such as phenyl, furyl, benzofuranyl, pyranyl, thienyl, pyrrolyl, and etc, does not reasonably provide enablement for the nitro-substituted aromatic carboxylic ester with any heteroaryl containing at least one heteroatom of N,O,S.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation, citing *Ex Parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,

- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breadth of the claims.

In the instant case, the claims encompass a process of making the nitro-aromatic carboxylic esters containing various heteroary groups. However,

Applicants' specification provide the only 11 examples ,which contain nothing about producing the nitro- aromatic carboxylic esters containing various heteroary groups. Accordingly, applicants ' specification is devoid of any synthetic procedures or directional guidance that would place said ring systems in possession of the public in view of an ultimate patent grant. Undoubtedly, more than routine experimentation would be involved to synthesize said ring systems. Compare *In re Armbruster*, 185 USPQ 152 (CCPA 1975); *In re Angstadt et al* , 190 USPQ 214 (CCPA 1976).

The specification, while being enabling for a tertiary amine base, such as triethylamine, tri-n-butylamine, and etc, does not reasonably provide enablement for all the tertiary amines. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to include the tertiary amines unrelated to the invention commensurate in scope with these claims. Therefore, an appropriate correction is required.

The specification, while being enabling for a phase-transfer catalyst, such as tetrabutylammonium bromide, tetrabutylammonium chloride, and etc, does not

reasonably provide enablement for all the phase-transfer catalysts. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to include all the phase-transfer catalysts unrelated to the invention commensurate in scope with these claims. Furthermore, catalyst compositions represent an unpredictable aspect in the art of organic chemistry. See *Ex parte Sizto*, 9 USPQ2d 2081 (Bd. Of App. And Inter. March 1988). Therefore, an appropriate correction is required.

Claims 24, 25, 30, 31, 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Phrases, "an aliphatic hydrocarbon", "an aromatic hydrocarbon", "acylic ether", "an acyclic ether", "a polar aprotic solvent", "a water-miscible solvent", "a water-immiscible organic solvent" are written. However, they are vague and indefinite. Each of them are unspecified as to the corresponding examples of the solvents. Therefore, an appropriate correction is required.

A phrase "a C₄-C₁₀ aryl or heteroaryl group" is written. However, this is vague and indefinite as to the range of the carbon atoms in the aryl group. The aryl group contains at least six carbon atoms in the compound. Therefore, an appropriate correction is required.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heck (U.S. 3,988,358) in view of Suto et al (U.S. 5,296,601).

Heck teaches a process of producing carboxylic acid esters by reacting aryl, heterocyclic, or benzylic halides or various substituted derivatives including a nitro group, an alkyl, or substituted halogen groups (see col. 1 ,lines 65-68) with carbon monoxide and an alcohol, such as methanol, ethanol , propanol, and etc. (see col. 2 ,lines 26-28) in the presence of a palladium catalyst and a tertiary amine selected from triethylamine, tri-n-butylamine (see col. 2 ,lines 49-51).

Furthermore, the reaction is carried out at a temperature in the range of from 20 to 175⁰ C. with a carbon monoxide pressure of from 1 to 10 atmospheres (see col. 2 ,lines 63-68) with the catalyst concentrations from 0.1 to 2 % (see col. 3 ,lines 15-17) in the presence of solvents, such as excess reactant alcohol, tetrahydrofuran, toluene, dimethylformamide (see col. 3 ,lines 3-5).

The instant invention ,however, differs from the Heck reference in that metal catalyst is a heterogeneous catalyst of palladium metal deposited on activated carbon.

Suto et al teaches a process of producing carboxylic acid esters by reacting an organic chloride represented by R^1Cl_m , where R^1 is a substituted or unsubstituted aromatic or heterocyclic hydrocarbon group and m is an integer of 1 or more, with R^4OH , where R^4 is a substituted or unsubstituted aliphatic, aromatic or heterocyclic

hydrocarbon group, carbon monoxide in the presence of a palladium compound ,such as metallic palladium, palladium carbon (see col. 4 ,lines 63-64) and a phosphine compound catalyst (see col. 1 ,lines 21-61) and a tertiary amine, such as triethylamine, tri-n-butylamine (see col. 5 ,lines 38-39).

Furthermore, the reaction is carried out at a temperature in the range of from 100 to 300⁰ C. with a carbon monoxide pressure of from 1 to 50 atmospheres (see col. 2 ,lines 63-68) in the absence or presence of solvents, such as hexane, benzene, ether, tetrahydrofuran, dimethylformamide (see col. 5 ,lines 50-53).

Heck does teach the process of producing carboxylic acid esters by reacting aryl, heterocyclic, or benzylic halides or various substituted derivatives including a nitro group, an alkyl, or substituted halogen groups with carbon monoxide and the alcohol in the presence of the palladium catalyst and the tertiary amine. Also, Suto et al does teach the process of producing carboxylic acid esters by reacting the organic chloride with the alcohol, carbon monoxide in the presence of metallic palladium or palladium carbon and the phosphine compound catalyst the tertiary amine. Both have commonly shared the process of producing carboxylic acid esters by reacting aryl halide with carbon monoxide and the alcohol in the presence of the palladium catalyst and the tertiary amine. Heck does disclose the use of the homogenous catalyst containing palladium in the process, whereas Suto et al expressly teaches the application of either the homogenous catalyst containing palladium or the heterogenous catalyst ,such as palladium carbon to the process. Thus, there is an equivalency between the use of

the homogenous catalyst and that of the heterogenous catalyst in the process of producing carboxylic acid esters. Therefore, it would have been obvious to the skillful artisan in the art to have motivated to incorporate a teaching of the Suto et al heterogenous catalyst into the Heck process in order to expand the limits of the homogenous catalyst, thereby economizing the overall process. This is because the skilled artisan in the art would expect the combined processes to have a similar success as shown in the Suto et al process.

Claims 28-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heck (U.S. 3,988,358) in view of Wehrenberg (U.S. 4,704,467) and Suto et al (U.S. 5,296,601).

Wehrenberg teaches a method of preparing mercaptobenzoates by reacting nitro-substituted aromatic carboxylic acid ester with a mercaptan (R-SH) (see from col. 1 line 55 to col. 2 , line 14) in the presence of an inorganic base ,such as potassium carbonate or sodium carbonate and non-polar aprotic solvents, such as benzene, tetrahydrofuran, diethyl ether, and a phase transfer catalyst including tetra-lower alkyl substituted ammonium and phosphonium halides (see col. 2 ,lines 28-40).

The instant invention ,however, differs from the Wehrenberg reference in that the intermediate reactants, carbon monoxide ,alcohol ,proton acceptor, and the heterogeneous catalyst of palladium metal deposited on activated carbon with its specific amount range, and the carbon monoxide pressure are unspecified. .

Heck teaches a process of producing carboxylic acid esters by reacting aryl, heterocyclic, or benzylic halides or various substituted derivatives including a nitro group, an alkyl, or substituted halogen groups (see col. 1 ,lines 65-68) with carbon monoxide and an alcohol, such as methanol, ethanol , propanol, and etc. (see col. 2 ,lines 26-28) in the presence of a palladium catalyst and a tertiary amine selected from triethylamine, tri-n-butylamine (see col. 2 ,lines 49-51).

Furthermore, Heck suggests that the reaction is carried out at a temperature in the range of from 20 to 175⁰ C. with a carbon monoxide pressure of from 1 to 10 atmospheres (see col. 2 ,lines 63-68) with the catalyst concentrations from 0.1 to 2 % (see col. 3 ,lines 15-17) in the presence of solvents, such as excess reactant alcohol, tetrahydrofuran, toluene, dimethylformamide (see col. 3 ,lines 3-5).

Moreover, Suto et al teaches a process of producing carboxylic acid esters by reacting an organic chloride represented by R^1Cl_m , where R^1 is a substituted or unsubstituted aromatic or heterocyclic hydrocarbon group and m is an integer of 1 or more, with R^4OH , where R^4 is a substituted or unsubstituted aliphatic, aromatic or heterocyclic hydrocarbon group, carbon monoxide in the presence of a palladium compound ,such as metallic palladium, palladium carbon (see col. 4 ,lines 63-64) and a phosphine compound catalyst (see col. 1 ,lines 21-61) and a tertiary amine, such as triethylamine, tri-n-butylamine (see col. 5 ,lines 38-39).

In addition, the reaction is conducted at a temperature in the range of from 100 to 300⁰ C. with a carbon monoxide pressure of from 1 to 50 atmospheres (see col. 2

,lines 63-68) in the absence or presence of solvents, such as hexane, benzene, ether, tetrahydrofuran, dimethylformamide (see col. 5 ,lines 50-53).

Wehrenberg does teach the method of preparing mercaptobenzoates by reacting the nitro-substituted aromatic carboxylic acid ester with a mercaptan (R-SH) in the presence of the inorganic base ,the non-polar aprotic solvent, and the phase transfer catalyst . Also, Heck does teach the process of producing nitro-substituted aromatic carboxylic acid esters by reacting various substituted aryl halides including a nitro group with carbon monoxide and the alcohol in the presence of the palladium catalyst and the tertiary amine. Moreover, Suto et al expressly teaches the equivalency between the homogenous catalyst and the heterogenous catalyst containing palladium in the process of producing the carboxylic acid esters.

In short, Heck does teach the preparation of the nitro-substituted aromatic carboxylic acid esters, the precursor of mercaptobenzoates , whereas Wehrenberg does teach the method of preparing mercaptobenzoates; they are connected to each other in the process.

Therefore, it would have been obvious to the skillful artisan in the art to have motivated to incorporate a teaching of Heck preparation step of producing nitro-substituted aromatic carboxylic acid ester carboxylic acid esters, along with the Suto et al heterogenous catalyst containing palladium, into the Wehrenberg process in order to make a single pot reaction process, thereby economizing the overall process with the reduction of unnecessary steps. This is because the skilled artisan in the art would

expect the combined processes to have a similar success as shown in the Wehrenberg process.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Scheben et al (U.S. 3,626,005) teaches a process of preparing unsaturated acyl halides by carbonylating vinyl halides in the presence of A Group VIII noble metal catalyst; acryloyl chloride is formed by reacting vinyl chloride with carbon monoxide in the presence of a palladium metal catalyst at a temperature of 25 to 300⁰ C. and a pressure of from 5 to 500 atmospheres.

Glenside et al (U.S. 3,729,508) teaches a synthesis of p-thiobenzoic acids by reacting halobenzoic acid with MSR in the presence of solvents, such as ethanol at a temperature of 0⁰ C..

Lentz et al (U.S. 4,507,493) teaches a process of preparing aryl carboxylic acids and derivatives by carbonylation of aryl sulfonyl chlorides. The aryl sulfonyl chlorides are reacted with carbon monoxide and water or an alcohol in the presence of a zero-valent metal catalyst containing palladium.

Lentz et al (U.S. 4,506,092) teaches a process of preparing aryl carboxylic acids and derivatives by carbonylation of triaryl sulfonium salts. The triaryl sulfonium salts are reacted with carbon monoxide and water or an alcohol in the presence of a triaryl phosphine and a zero-valent metal catalyst containing palladium.

Suto et al (U.S. 5,142,057) teaches a process of producing carboxylic acid esters by reacting an organic chloride with R^4OH and carbon monoxide in the presence of a palladium compound and a phosphine compound catalyst, and a tertiary amine.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 703-305-0809. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 703-308-4698. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-2742 for regular communications and 703-305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

April 15, 2003


ALAN L. ROTMAN
SUPERVISORY PATENT EXAMINER
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